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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,543	02/17/2004	Moshe Flashner-Barak	1662/63202	3365

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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/781,543	FLASHNER-BARAK ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *7-19 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/27/04;12/27/04;06/21/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-21 are presented for examination.

Acknowledgement is made of Applicant's claim for benefit under 35 U.S.C. 119(e) to U.S. Provisional Patent Application No. 60/449,246, filed February 20, 2003.

Applicant's Information Disclosure Statements (IDS) filed May 27, 2004 (two pages), December 27, 2004 (one page) and June 21, 2007 (one page) have each been received and entered into the present application. As reflected by the attached, completed copies of form PTO-1449 (four pages total), the Examiner has considered the cited references.

Applicant's response filed November 6, 2007 to the requirement for restriction/election dated June 20, 2007 has been received and entered into the present application. Pursuant to the new requirement for restriction/election issued January 16, 2008, the previous requirement for restriction/election dated June 20, 2007 was vacated. Applicant's response filed March 17, 2008 to the requirement for restriction/election dated January 16, 2008 has also been received and entered into the present application.

Requirement for Restriction/Election

Applicant's election **with traverse** of the invention of Group I (claims 1-6), directed to a composition for improving the bioavailability of a drug comprising at least one poorly bioavailable drug dissolved in an effective amount of menthol; the election of the genus of "drugs with low aqueous solubility" as the at least one poorly bioavailable drug and the species of cyclosporine as the specific drug with low aqueous solubility, in the reply filed March 17, 2008, is acknowledged by the Examiner. In view of the fact that instant claim 20 has been newly added and depends from instant claim 1, examination of the elected group (claims 1-6) will now also include examination of newly added claim 20.

Applicant traverses the requirement on the grounds that examining claims 1-21 as a single group would not place a serious burden on the Examiner because all of the instant claims are directed to compositions for improving the bioavailability of a drug that includes menthol and the use of such compositions for improving the bioavailability of a drug, reducing the variability of the bioavailability of a drug, and increasing the extent of time that the drug provides a therapeutically significant concentration in the blood or plasma. Applicant alleges that the claims are sufficiently similar to make it possible to examine them together with minimal search due to the extensive overlap of prior art.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Though Applicant may be correct in stating that Inventions I-IV are related in the sense that each employs a composition of a drug that includes menthol, it remains that, despite this commonality between the inventions, each invention is distinct from the others on the grounds that the inventions each have distinctly different objectives, endpoints and steps that may be used to accomplish the various materially different methods of use as claimed. As shown at pages 2-10 of the requirement for restriction/election dated January 16, 2008, the different inventive groups designated as Groups I-IV are directed each to distinct subject matter, each method having distinct methodologies and effects. Notwithstanding that some of the methods may have overlapping steps, the scope of each invention is not necessarily co-extensive with any one or more other inventions and, thus, a reference that would anticipate or render obvious claims of one invention would not necessarily anticipate, suggest or render obvious the invention of any one or more of the other claimed inventions. In light of such, performance of a comprehensive search for one of the methods would not necessarily result in a complete or comprehensive search for any one or more of the other methods. Furthermore, consideration of the findings of such a search in accordance with the requirements of the law under 35 USC §§ 101, 102, 103 and 112 would be unduly burdensome in view of the distinct nature of each of the inventions and the fact that the issues raised with regard to one single invention would not necessarily be applicable to any one or more of the other claimed

inventions in view of the difference in claim scope. In view of these facts, the distinctness of each of the inventions is firmly grounded in the guidance provided in the MPEP at §806.05(j) and is herein properly maintained

Applicant is also reminded that, with regard to the present election of species requirement, the species elections were set forth for examination purposes and, should the elected species be found allowable, search and examination will be expanded to other claimed species of (a) drug with low aqueous solubility and (b) at least one poorly bioavailable drug.

Therefore, for the reasons above and those made of record at pages 2-10 of the previous Office Action dated January 16, 2008, the requirement remains proper and is hereby made **FINAL**.

Claims 7-9 and 21 are **withdrawn** pursuant to 37 C.F.R. 1.142(b) as being drawn to non-elected subject matter.

The claims corresponding to the elected subject matter are claims 1-6 and 20 and such claims are herein acted on the merits.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description Requirement, New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Present claim 20 is directed to a composition for improving the bioavailability of a drug comprising at least one poorly bioavailable drug dissolved in an effective amount of menthol, wherein the

effective amount of menthol is about 20% to about 99% by weight of the composition, wherein the improvement in bioavailability is determined as at least a 5% increase in the ratio of AUC_t/AUC_r above 100%.

In particular, the specification and claims as originally filed fail to provide adequate written description for the newly added limitation directed to wherein the improvement in bioavailability is determined as at least a 5% increase in the ratio of AUC_t/AUC_r above 100% (claim 20).

MPEP §2163 states, "The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test of sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983))…Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)."

Applicant discloses at p.6, l.28-p.7, l.11, "As used herein, the term 'improving bioavailability' refers to the increase in concentration of a drug as compared to the concentration of the drug without

menthol. In other words, drug bioavailability is proportional to, and is typically measured by, the total area under the curve (AUC) of the concentration of the drug found in blood or plasma versus time when measured in a pharmacokinetic trial in a human or an animal. The AUC may be expressed as AUC_t, *i.e.* the area under the curve to the last measured time point, or AUC_i, *i.e.* the area under the curve extrapolated to infinite time. The improvement in bioavailability is measured by the percent increase in the average AUC of the subjects in the trial when dosing the drug dissolved in menthol as compared to the average AUC of the same subjects obtained by standard dosing of the drug. Alternately, the AUC ratio of the test formulation (AUC_t) to the AUC of the reference formulation (AUC_r) may be calculated on a per subject basis and then averaged. A percent of the average ratio (AUC_t/AUC_r) above 100% is then the improvement in bioavailability. Typically, the improvement in the average AUC obtained by standard dosing of the drug is about 5%, and preferably, the improvement is about 10% or more in the bioavailability, which is considered significant."

However, such disclosure of the improvement in bioavailability measured by a percent increase in the average AUC using the drug dissolved in menthol compared to the average AUC obtained by standard dosing [i.e., using the ratio (AUC_t/AUC_r)], wherein the improvement in the bioavailability is preferably increased *about* 5% above 100%, fails to provide adequate written support to now claim (1) the improvement in bioavailability determined by a increase in the ratio of (AUC_t/AUC_r) above 100% or (2) wherein the improvement is "at least a 5% increase". This is a clear broadening of the subject matter both claimed and disclosed in the specification and claims as originally filed that is not adequately supported, either explicitly or implicitly, by the original disclosure because the original disclosure of measuring the improvement in bioavailability using the average ratio of (AUC_t/AUC_r) (wherein AUC_t is the area under the curve using the test formulation and AUC_r is the area under the curve using the reference formulation) fails to provide written support to now claim that the improvement in bioavailability is determined using the ratio (AUC_t/AUC_r) (wherein AUC_t is the area under the curve measured to the last time point and

AUC_T is the read under the curve using the reference formulation). It is clear, therefore, that Applicant was not in possession of the concept of determining the improvement in bioavailability using the ratio of (AUC_T/AUC_R) as now claimed, but rather was solely in possession of the concept of determining the improvement in bioavailability using the ratio of (AUC_T/AUC_R) as originally disclosed.

Furthermore, the disclosure of an "about 5%" improvement in bioavailability fails to provide adequate written support to now claim an "at least" 5% improvement in bioavailability. This is a clear narrowing of the subject matter both claimed and disclosed in the specification and claims as originally filed that is not adequately supported, either explicitly or implicitly, by the original disclosure because the disclosure of "about 5%" permits variation both above and below the designated endpoint of 5%, whereas the newly claimed limitation of "at least" 5% permits values of 5% or greater. It is clear, therefore, that Applicant was not in possession of the concept of determining an improvement in bioavailability as "at least a 5% increase in the ratio of (AUC_T/AUC_R) above 100%", but rather was solely in possession of the concept of determining an improvement in bioavailability as an about 5% increase in the ratio of (AUC_T/AUC_R) above 100%, as evidenced by the original filed disclosure at p.6, l.28-p.7, l.11.

As stated in MPEP §2163, "The subject matter of the claim need not be described literally (i.e., using the same terms of *in haec verba*) in order for the disclosure to satisfy the description requirement." However, considering the teachings provided in the specification as originally filed, Applicant has failed to provide the necessary teachings, by describing the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that Applicant had possession of the limitation directed to wherein the improvement in bioavailability is determined as at least a 5% increase in the ratio of AUC_T/AUC_R above 100% (claim 20).

Accordingly, the claim is considered to lack sufficient written description and is properly rejected under 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 3 is directed to a composition for improving the bioavailability of a drug comprising at least one poorly bioavailable drug dissolved in an effective amount of menthol, wherein the effective amount of menthol is about 20% to about 99% by weight of the composition, and further wherein the drug with low aqueous solubility is a drug having a water solubility of less than about 20 mg per milliliter of water.

In particular, the term "less than about" renders the scope of the claim indefinite because the term "less than" denotes a specific and fixed endpoint (i.e., that the composition has an aqueous solubility of less than 20 mg/mL), but the term "about" permits variation both above and below the endpoint of 20 mg/mL. As a result, the terms conflict since it is unclear which term is meant to be limiting (i.e., either "less than" or "about"). For these reasons, the metes and bounds of the subject matter for which Applicant is presently seeking protection are not clearly defined.

For these reasons, the claim fails to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and is, thus, properly rejected.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 6 is directed to a composition for improving the bioavailability of a drug comprising at least one poorly bioavailable drug dissolved in an effective amount of menthol, wherein the effective amount of menthol is about 20% to about 99% by weight of the composition, and further

wherein the compound is cyclosporine.

In particular, there is insufficient antecedent basis for the limitation "the compound" as recited in line 1 of claim 6, since independent claim 1 from which claim 6 depends fails to set forth any reference to a "compound" *per se*.

For these reasons, the claim fails to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and is, thus, properly rejected.

For the purposes of examination, the limitation "the compound" as recited in claim 6 will be interpreted to further define the "at least one poorly bioavailable drug" as recited in instant claim 1.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 20 is directed to a composition for improving the bioavailability of a drug comprising at least one poorly bioavailable drug dissolved in an effective amount of menthol, wherein the effective amount of menthol is about 20% to about 99% by weight of the composition, and further wherein the improvement in bioavailability is determined as at least a 5% increase in the ratio of AUC_I/AUC_T above 100%.

In particular, there is insufficient antecedent basis for the limitation "the ratio" as recited in line 2 of claim 20, since independent claim 1 from which claim 20 depends fails to set forth any reference to "a ratio" *per se*.

For these reasons, the claim fails to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and is, thus, properly rejected.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Benet et al. (U.S. Patent No. 6,121,234; 2000) in light of Ran et al. ("Solubilization of Cyclosporin A", *AAPS PharmSciTech*, 2001; 2(1); 1-4) and PDR for Herbal Medicines (p.628-631; 2004), each cited to show facts.

Benet et al. teaches increasing bioavailability and reducing inter- and intra-individual variability of an orally administered hydrophobic pharmaceutical compound by orally co-administering the pharmaceutical compound to a mammal in need of treatment with the compound in combination with an essential oil or essential oil component in an amount sufficient to provide bioavailability of the compound in the present of the essential oil greater than the bioavailability of the compound in the absence of the essential oil or essential oil component (abstract). Benet et al. teaches that the essential oil used generally will increase drug bioavailability by at least 10%, preferably by at least 50%, and more preferably by at least 75% of the difference between bioavailability in the presence of the essential oil and total bioavailability of the ingested dosage in the absence of the essential oil [col.19, l.4-12; i.e., meets Applicant's claimed limitation of instant claim 20, which requires the at least a 5% increase in bioavailability of the test formulation (i.e., the formulation of drug plus essential oil) as compared to the reference formulation (i.e., the formulation of drug in the absence of essential oil)]. Exemplary formulations are disclosed at Table 4 (col.27), wherein exemplary formulation A comprises, *inter alia*, 100 mg cyclosporin (instant claims 1-6) as the pharmaceutical agent and 100 mg peppermint oil as the essential oil component, adding to a total weight of 700 mg.

Ran et al. is cited to show that the aqueous solubility (i.e., water solubility) of cyclosporine is 27.67 μg/mL at 25°C (col.2, para.1, p.1), which meets Applicant's instantly claimed limitation of instant claim 3 directed to a drug having a water solubility of less than about 20 mg/mL of water. Citation to this reference is made in accordance with MPEP §2131.01, which states that it is proper to rely upon a secondary reference for a rejection under 35 U.S.C. 102 provided that the additional reference is relied upon to demonstrate that a characteristic or property not disclosed by the primary reference is, in fact, inherent.

PDR for Herbal Medicines (p.628-631; 2004) is cited for its teaching that peppermint oil contains 35-45% menthol (col.2, para.4, p.628). Citation to this reference is made in accordance with MPEP §2131.01, which states that it is proper to rely upon a secondary reference for a rejection under 35 U.S.C. 102 provided that the additional reference is relied upon to demonstrate that a characteristic or property not disclosed by the primary reference is, in fact, inherent.

Accordingly, 100 mg peppermint oil as contained in exemplary formulation A would contain 35-45 mg menthol, which, for a formulation of 700 mg total weight, would be equivalent to 5-6.4% by total weight of the composition. Though it is noted that this percentage is less than "about 20%" as instantly claimed (instant claim 1), this teaching of 5-6.4% menthol by total weight of the composition is understood to meet Applicant's claimed amount of menthol of "about 20%" (claim 1) because the term "about" as used in instant claim 1 permits some tolerance both above and below the recited endpoint absent an explicit definition of the degree of variation intended to be encompassed by the term. Where close prior art exists (such as, in this case, Benet et al.), the burden is on Applicant to establish that the term "about" as used in the instant claims is sufficiently clear to avoid such art. In the instant case, Applicant has failed to provide a definition of the term "about" in the instant specification, such that there is no indication or hint as to what amount of variation above or below the recited amount would constitute infringement of the instant claims. There is nothing in the specification, prosecution history or prior art

that provides any indication as to what amount of variation is tolerated by the term "about". Absent such information, and further in view of what is actually disclosed by Benet et al. (i.e., menthol in an amount of 5-6.4% total weight of the disclosed composition), this teaching in Benet et al. is understood to meet Applicant's claimed amount of "about 20%" (claim 1), absent factual evidence to the contrary, and further absent any clear indication in the specification or claims that an amount of 5-6.4% would not be encompassed by the variation in and around the claimed endpoint of "about 20%" (claim 1).

Regarding the application of the PDR of Herbal Medicines as factual evidence, Applicant is directed to MPEP §2124, which teaches that in certain circumstances, a factual reference need not antedate the filing date of the instant application. Specifically, "In certain circumstances, references cited to show a universal fact need not be available as prior art before applicant's filing date. *In re Wilson*, 311 D.2d 266, 135 USPQ 442 (CCPA 1962). Such facts include the characteristics and properties of a material or a scientific truism." Accordingly, the reference is properly relied upon, despite the fact that it was published in 2004, because it teaches a well-known scientific fact, i.e., the percentage by weight of menthol in peppermint oil.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10 and 16-17 of U.S. Patent Application No.

11/357,757.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claims are either anticipated by, or would have been obvious over, the reference claims.

Although the conflicting claims are not identical, the claims of the instant patent application and those of the copending patent application or patents are not considered patentably distinct from each other because the copending claims render the present claims obvious.

The copending claims provide for a pharmaceutical composition comprising microparticles of cyclosporine (copending claim 10) obtained from sublimation of a sublimable carrier, such as, *inter alia*, menthol (copending claims 16-17), using a solid solution of cyclosporine in the sublimable carrier (copending claim 10). In other words, the copending claims clearly provide for a composition of microparticles of cyclosporine coated in the sublimable carrier menthol.

The copending claims fail to teach the composition (1) for improving the bioavailability of the cyclosporin (instant claim 1) or (2) menthol in an amount of about 20% to about 99% by weight of the composition (instant claim 1).

Regarding the fact that the copending claims fail to explicitly teach the claimed composition for improving the bioavailability of cyclosporin, this limitation of the instant claims fails to patentably distinguish the instant claims over the copending claims because the limitation of present claim 1 describing the composition "for improving the bioavailability of a drug" is an intended use of the composition (i.e., an intent to use the disclosed composition for improving the bioavailability of the cyclosporin), which does not impart any physical or material characteristic to the composition that is not already present in the copending claims. If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended

use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble of not considered a limitation and is of no significance to claim construction. See *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.2d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999). See also *Rowe v. Dror*, 112 F.3d 473, 378, 42 USPQ2d 1550, 1554 and MPEP §2112.02(II). In the instant case, the copending claims meet each and every structural and physical limitation of the instantly claimed composition and, thus, would be reasonably expected to be capable of performing the intended use as instantly claimed, absent factual evidence to the contrary and further absent any apparent structural difference between the composition of the copending claims and that of the instant claims.

Regarding the use of menthol in an amount of about 20% to about 99% by weight of the composition, the determination of the optimal amount of menthol would have been a matter well within the purview of, and *prima facie* obvious to, one of ordinary skill in the art at the time of the invention. Such a determination would have been made in accordance with a variety of factors, the desired concentration of cyclosporine in the menthol carrier, the amount of cyclosporine necessary for therapeutic use to be dissolved in the menthol carrier, the solubility of cyclosporine in the menthol carrier, etc. Thus, the amount that would have actually been employed would have varied widely and, in the absence of evidence to the contrary, the currently claimed specific amounts are not seen to be inconsistent with that which would have been determined by, and well within the routine skill of, the skilled artisan.

Additionally, the concentration of the active ingredients is a result-effective variable, i.e., a variable that achieves a recognized result, and, therefore, the determination of the optimum or workable dosage range would be well within the practice of routine experimentation by the skilled artisan, absent factual evidence to the contrary, and, further, absent any evidence demonstrating a patentable difference between the compositions used and the criticality of the amount(s). In further support thereof, Applicant's attention is directed to the MPEP at §2144.05, which states, "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed

set of percentage ranges in the optimum combination of percentages...Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."

Accordingly, rejection of claims 1-6 is proper over claims 10 and 16-17 of U.S. Patent Application No. 11/357,757 as claiming obvious and unpatentable variants thereof.

Conclusion

Rejection of claims 1-6 and 20 is proper.

Claims 7-19 and 21 are **withdrawn** from consideration pursuant to 37 C.F.R. 1.142(b).

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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